AD-A271 872

REPORT DOCUMENTATION PAGE

Form Approved
OMB No 0704-0188

(2)

2. REPORT DATE	19 Oct 93
3. REPORT TYPE AND DATES COVERED	Final 15 Feb 90 to 14 Feb 93
4. TITLE AND SUBTITLE	COGNITION AND THE BRAIN: A CONTINUATION OF THE UNIVERSITY RESEARCH INITIATIVE AT NEW YORK UNIVERSITY
5. FUNDING NUMBERS	61102F AFOSR 90-0221 2313 BS
6. AUTHOR(S)	Dr Lloyd Kaufman
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	Dept of Psychology and Neural Science New York University 15 Washington Place New York, NY 10003
8. PERFORMING ORGANIZATION REPORT NUMBER	AEOSR-TR- 18
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	AFOSR/NL 110 Duncan Avenue, Suite B115 Bolling AFB DC 20332-0001 Dr John Tangney
10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES	
12a. DISTRIBUTION/AVAILABILITY STATEMENT	Approved for public release; distribution unlimited
12b. DISTRIBUTION CODE	

13. ABSTRACT *(Maximum 200 words)*

The main focus of this project was the make use of magneto encephalographic (MEG) measures of brain activity to determine how the brain's neural resources are deployed during various cognitive tasks entailing different degrees of mental workload. Our laboratory pioneered this field, and the methods it devised are presently in wide use in clinical applications, as well as in other research laboratories. We initiated the use of a simple procedure to fit observed extracranial field patterns to fields that would be produced by equivalent current dipoles. The ideal dipole's position, orientation and strength (current dipole moment) was adjusted until its field pattern matched that of the observed pattern. This is a primitive form of what we now refer to as *Magnetic Source Imaging* (MSI). It is still the basic method in clinical applications, but a more sophisticated form of MSI is now emerging, largely as a result of work on this project.

14. SUBJECT TERMS	
15. NUMBER OF PAGES	9
16. PRICE CODE	

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
(U)	(U)	(U)	(UL)

NSN 7540-01-280-5500

Standard Form 298 (Rev 2-89)
Prescribed by ANSI Std Z39-18

delim $$
gsize 11
gfont R

COGNITION AND THE BRAIN

A Final Technical Report Submitted to the
U.S. Air Force Office of Scientific Research

by Lloyd Kaufman, Professor of Psychology and Neural Science

New York University

Introduction

This is the Final Technical Report on Grant No. AFOSR 90-0221 entitled "Cognition and the Brian". It covers the period from 15 February 1990 through 14 February 1993. A total of 22 papers were completed during this time. Twenty of these papers are already in print, with the remaining two submitted for publication. Another paper is still in preparation, and is nearing completion. Of the papers already in print, 13 appeared in peer review journals and the remaining appeared in proceedings of conferences. (Some of these are also subject to peer review). Reprints and preprints of all of these papers were previously submitted to AFOSR and to its prescribed mailing list.

The main focus of this project was the make use of magnetoencephalographic (MEG) measures of brain activity to determine how the brain's neural resources are deployed during various cognitive tasks entailing different degrees of mental workload. Our laboratory pioneered this field, and the methods it devised are presently in wide use in clinical applications, as well as in other research laboratories. We initiated the use of a simple procedure to fit observed extracranial field patterns to fields that would be produced by equivalent current dipoles. The ideal dipole's position, orientation and strength (current dipole moment) was adjusted until its field pattern matched that of the observed pattern. This is a primitive form of what we now refer to as *Magnetic Source Imaging* (MSI). It is still the basic method in clinical applications, but a more sophisticated form of MSI is now emerging, largely as a result of work on this project. Nevertheless, the earlier form of MSI is still useful despite its limitations (see below and also Williamson and Kaufman, 1987).

First we describe the uses of the earlier form of MSI in connection with studying cognition. It is possible to routinely record the extracranial magnetic field associated with the flow of ionic currents within neurons of the cerebral cortex. The intervening tissues are esentially transparent to the component of the field normal to the scalp. This makes it relatively simple to locate the region of cortex within which neuronal activity gives rise to the field. Since these measures have a temporal resolution of a fraction of a second, it is now possible to noninvasively determine the temporal sequences of activation of what Goldman-Racic (1988) described as cortical *networks*. This is not possible with any of the other better known functional imaging modalities.

It is to be noted that knowledge of brain anatomy is not required for computing the location of the source modelled as a current dipole. Rather, point dipole parameters are computed from the field at the scalp. The dipole is localized within the three-dimensional volume inside the head. These equivalent current dipole sources are then superimposed on the image of the brain. In one experiment (Romani et al., 1982a) point dipole sources that account for fields evoked by tones of different pitch were located along the floor of the lateral sulcus near Heshl's gyrus. Romani et al. found a log-linear relationship between tone frequency and distance along the cortex. The slope of the function relating log frequency to distance was approximately 3 mm/octave. This is consistent with the finding (Yamamoto et al., 1988) that point dipole's may be localized within a circular position error of less than 3 mm in repeated series of measurements. Also, given the position distance of the equivalent current dipole from the surface, the strength of its tangential component (the current dipole moment) can be computed precisely. Assuming that the dipole is oriented normal to the surface of the cortex, then its total strength (radial and tangential components) may also be determined (Romani et al., 1982b). This very early contribution of our laboratory was the first determination of the tonotopic sequence on the human auditory cortex, and it has since been confirmed in several laboratories. This experiment set the standard for the work done at the outset of this project.

Experimental Studies of Echoic Memory

Lu, Williamson, and Kaufman (1992) discovered two temporally overlapping sources of the N100 component of the auditory response. One is located in primary auditory cortex, and the other in association cortex. Despite many years of work with N100, and an influential paper by Naatanen and Picton (1987) postulating the contributions of multiple sources to N100, no ERP study succeeded in identifying any of them. This study, which was published in *Brain Research*, demonstrated that the excitability of primary auditory cortex increases exponentially with time after presentation of a tone. Furthermore, the source in association cortex has its own distinct lifetime.

It is well known that the amplitude of N100 increases with ISI. This is also true of the magnetically detected N100 arising from primary auditory cortex. In a second paper, Lu, Williamson, and Kaufman (1992) describe an experiment in *Science* in which the lifetime of the change in amplitude of the ERF with ISI is the same as the lifetime of echoic memory, as measured behaviorally. Therefore, the ERF due to sources in primary auditory cortex of both hemispheres indicates the state of that region of the brain subsequent to stimulation. This state reflects the passive echoic memory which is often described as the first stage in cognition.

Studies of Attention

Luber, Kaufman, Williamson, and Moeller (1993) completed a paper based on work supported by this project. That paper is submitted for publication. It examined the effects of selective attention to locations in visual space on sources within the cortex. Again, the sources were modelled as current dipoles. At least two such sources were found in each hemisphere. Those that responded with a latency of less than about 240 msec exhibited the usual effect of attention. That is, when subjects were instructed to attend to a particular location in visual space, stimuli at that location evoked responses of larger amplitude than stimuli at ignored locations. However, it was also found that the mere instruction to attend created this effect, even if the instruction had no effect whatsoever on performance of a simple task. Alternatively, later components were also differentially affected by attention. However, this effect occurred if and only if the instruction to attend resulted in a measurable improvement in performance. When the paper is finally accepted by a peer review journal, copies will be remitted to AFOSR.

Cognition and Ongoing Brain Activity

Other work supported by this project (cf. Wang, Williamson, and Kaufman 1992; Wang, Kaufman, and Williamson, 1992) laid the foundations for the newer and more sophisticated form of MSI. It demonstrated that sources of activity can be uniquely described without assuming any specific source model provided that adequate knowledge of the underlying anatomy is available. State-of-the art MRI equipment is now capable of providing that information. This is a major outcome of the project. It proves that the pattern of current giving rise to the observed field can now be inferred without making prior assumptions about the nature of the source.

Much of this work for AFOSR was motivated by our finding that the ongoing (spontaneous) activity of the brain is locally modulated by the mental activity in which the subject is engaged (Kaufman, Schwartz, Salustri, and Wiliamson (1990). These changes in the background brain activity are not revealed by conventional signal averaging. Nor can they be clearly observed in the ongoing magnetoencephalogram (MEG). The basic method of extracting the variance around the average response within limited bands of MEG activity is described in Kaufman et al. (1990), as well as in the papers by Kaufman, Kaufman, and Wang (1991) and by Kaufman, Curtis, Wang and Williamson (1992), which were also supported by this project. The latter paper is particularly interesting as it shows that scanning short term memory is closely linked to changing levels of activity of particular cortical regions and may thus provide information similar to that provided by blood flow measures, except in a finer scale of temporal resolution.

Work on this project clearly indicates that classic evoked responses - potentials or fields - are important but incomplete indices of higher cognitive processes. To understand cognition we must also study the ongoing (intrinsic) brain activity and how it is modulated by cognitive processes. Apparently this modulation denotes the engagement of different parts of the cortex in different cognitive tasks. Work in this area has barely begun, and it should be supported. This was recently the focus of a meeting on Brain Oscillations held in Tecklenberg, Germany during the first week of September of 1993. AFOSR did not support this important conference.

On the Inverse Problem

In still other work supported by AFOSR, Kaufman, Kaufman, and Wang (1991) demonstrated that accurate knowledge of the geometry of the underlying cortex makes it possible to account for the distribution of field power, and to locate cortical regions whose activity is affected by mental processes. This is the first paper to clearly state that the geometry of the cortex plays a vital role in determining the nature of the extracranial field (and the scalp potential). This is one of the most important contributions of the project, as it proves conclusively that under many circumstances statements about brain activity based solely on the electric or magnetic phenomena detected at the scalp can be essentially meaningless unless the geometry of the underlying cortex is taken into account. We shall see later how these considerations led to the proof that a unique solution to the inverse problem may be found.

The more sophisticated form of MSI dispenses with the current dipole model and instead delineates the boundary of the active region, as well as the strength of activity within the region. It is important to note that this second type of MSI has only been explored in computer simulations, and part of this project, of continued, would have been to extend the method to real brains.

Implementing the second type of MSI depends upon having an accurate 3-dimensional representation of the cortex of each subject's brain. The coordinates and orientations in 3-dimensions of the finite elements or the normal to the splines that might be used to define the cortical surface are essential to this computation. Hence, unlike the passive role played by imagery in the simpler kind of MSI, the process of magnetic source imaging necessarily entails integrating anatomical data with magnetic field data (i.e., the spatio-temporal distribution of the extracranial magnetic field). This is a computer-intensive task, and the code developed to implement it will probably have to be parallelized. However, this work was halted with the termination of our project and, to our knowledge, is not being pursued elsewhere in the world at this time. Why is it important that this be done?

Many issues in cognitive psychology cannot be resolved from behavioral data alone. This refers to controversies in the field of mental imagery, as well as whether short-term memory search is seqquential, parallel, or some combination of both. Most of the current theories seem to be able to account for the behavioral data. However, direct measures of brain activity can play an important role in resolving these problems. For example, does mental imagery entail manipulating neural representations of visual objects, or does it involve manipulating neural representations of abstract propositions about the objects (cf. Finke & Shepard, 1986; Pylyshyn, 1973; Kosslyn, 1983)? It may not be possible to generate behavioral data that can decisively distinguish among these alternative views of mental imagery (cf. Anderson, 1978). However, measures of brain activity could reveal the action of *neural networks* (Goldman-Racic, 1988) involved in imagery as well as networks involved in other equally demanding cognitive tasks. As we shall see, the activation of neural networks can be identified using MSI.

Regional cerebral blood flow (rCBF) data collected while subjects imagined walking in their own neighborhoods support the view that imagery involves the visual system (Roland & Friberg, 1985). The data indicate increased blood flow in occipital cortex, posterior parietal lobe, and in posterior inferior temporal lobe. Other experiments using SPECT rather than rCBF reveal that right parietal and right frontal lobes exhibit relatively increased blood flow as subjects engage in other imaging tasks (Goldenberg et al., 1989). Our own magnetoencephalographic (MEG) studies conducted under AFOSR support on this project revealed a verbal component, as evidenced by activity in the left fronto- temporal area similar to that found when subjects engage in a purely verbal task. However, we also observed differential activity in occipital cortex and right frontal, as did the blood flow studies (Kaufman, Cycowicz, Glanzer, and Williamson, 1993). Furthermore, work by Michel, Kaufman, and Williamson (1993) shows that nearly 90% of the variance in the reaction time data obtained in a replication of the Cooper-Shepard mental rotation task is accounted for by changes in levels of ongoing activity of occipital cortex. This work is accepted for publication in a refereed journal.

Farah and her colleagues (1988) used the visual event related potential (ERP) to localize effects of mental imagery. Their subjects were told to imagine a letter. e.g., "H".

prior to visual presentation of the letter. The 200 msec latency ERP component measured over the occipital and parietal areas was enhanced in amplitude when the "H" was the actual stimulus. Farah concluded that both mental imagery and visual perception share a common neural substrate. Our results are consistent with those of Farah et al. However, the activity of several non-occipital regions in different imaging tasks revealed in blood flow studies and with MEG was not detected in the ERP study. The conventional ERP study is not designed to resolve such underlying complexity. Moreover, the ERPs did not reflect the time required for the completion of this cognitive task.

Event related fields (ERFs) are of short duration relative to the time needed to complete many imaging tasks. Therefore, as suggested by studies of blood flow and of changes in level of intrinsic activity, neither ERPs nor ERFs fully reflect the neural activity that goes on during performance of these tasks. However, event related responses can signal onsets of some of these processes as well as the state of the responding tissue at the time of the onset. Similarly, measures of blood flow indicate that some regions become more or less active at some time during performance of these task. They cannot reveal the durations of these activities, nor the temporal sequences of their occurrences. Temporal resolution of metabolic measures using, e.g., deoxyglucose, is even coarser than PET measures of blood flow. However, temporal information can be retrieved from time-varying topographic maps of MEG activity and these maps can be used to determine the cortical loci of the sources of this activity.

As recounted above, the power of the extracranial field in the alpha band undergoes changes depending upon the nature of the task being performed. Thus, searching memory for a previously seen item results in a temporally commensurate reduction in alpha power (Kaufman, et al., 1989). This alpha suppression is normally construed to be equivalent to cortical *activation*). Memory search for previously heard tones results in a correlated activation of right temporal cortex (Kaufman et al., 1991), and not of occipital alpha.

Changes in levels of intrinsic neural activity can be measured with a temporal resolution of a fraction of a second. Further, when measured over the appropriate cortical region the duration of activation coincides with the time needed to signify completion of the search. Moreover, when different regions are involved, as when performing a verbal task based on the presentation of a visual word, the activation of visual cortex precedes subsequent activation of left fronto-temporal cortex. Thus, MEG measures of activation are known to covary with many cognitive processes. Unfortunately, we are unable to continue this line of work.

The local changes in spontaneous activity which we found to be related to ongoing cognitive processes cannot be treated in the same way as are coherent components of event related fields. However, local changes in average field power within a given MEG band also benefit from the fact that only nearby sources affect the pick-up coils. So, to a first approximation, it is possible to identify the region of cortex whose activity is modified by the cognitive task. However, our theoretical work in this area proves that it is possible to delineate the actual shape of the cortical area whose activity is affected by cognitive tasks.

A classic problem in EEG, EKG, and MEG is the so-called *inverse problem*, which in general it has no unique solution since it is ill-conditioned, but it can have several solutions. Why must be introduced is constraints which select from the larger number of possible solutions a smaller number which not only satisfy the measured fields but also satisfy the additional constraints. Many different sources can be deduced to account for an observed distribution of fields or potentials. However, many investigators are aware of the fact that this problem may be minimized provided that one has prior constraining knowledge of possible source locations. This is particularly true of the cortex, which can be treated as though it is a uniformly thick membrane, where all current elements flow normal to its surface. In fact, Kaufman et al. (1991) demonstrated that the geometry of a folded "cortex" populated with such current elements has a profound effect on the extra-cranial field to which these elements give rise. The geometry alone is of such great importance that unless it is taken into account one cannot distinguish between synchronized or desynchronized cortical activity based on the scalp-detected EEG or MEG alone.

In the papers completed under this project by Wang et al. (1992a,b,c), we demonstrated that accurate prior knowledge of cortical geometry makes it possible to derive a mathematically unique solution to the inverse problem. The geometry is available in state-of-the art MRI scans. MRI slices may be used to construct accurate 3-dimensional representations of the cortex, and the observed field pattern related uniquely to extended distributions of active current elements. Furthermore, we extended the method to cover situations in which ongoing spontaneous brain activity is either enhanced or diminished by some ongoing mental task. Analysis of the average field power distribution about the scalp, together with knowledge of the cortical geometry, permits calculation of the distribution of cortical current power underlying the observed average field power pattern. Since these patterns may change rapidly with time, and often shift across the surface of the scalp from one brain region to another, the temporal resolution afforded by MEG makes it possible to develop a dynamic functional image of brain activity. If our work on this problem had been permitted to continue, we would have developed this technique to provide dynamic functional images of the human brain as it undertakes various cognitive tasks.

We had made a start in this direction under this project. Since accurate knowledge of the brain's geometry is essential, we undertook the reconstruction of one subject's brain from MRI slices. The scan was of the PI's brain. It was made by Dr. Thomas Budinger of the Berkeley Lawrence Laboratory using state-of-the art equipment at the University of Pennsylvania. The Air Force project did not pay for this service, which was provided *gratis*. The PI then undertook the segmentation of cortex from the slices using software developed at the NYU Medical Center by Dr. M. Noz of the Department of Radiology. This required several weeks of work. Since funds for this type of work were cut off, this and other attempts at reconstruction were suspended indefinitely. Nevertheless, it should be noted that many person-hours went into this effort although the support for this work had already been withdrawn by AFOSR.

Conclusions

Overall, this was an enormously productive project. With a work force and budget of minimum size, we managed to produce a large number of experimental and theoretical results of considerable importance to cognitive neuroscience. We made truly important advances in the field, and were on the threshold of making even greater strides when the project concluded. It is our hope that some other group will take up where we left off to complete the task that is now so clearly laid out.

References

Anderson, J.R. Arguments concerning representations for mental imagery. *Psychol. Rev.* 1978, 85, 249-277.

Cycowicz, Y., Kaufman, L., Glanzer, M. & Williamson, S.J. Selective suppression of spontaneous cortical rhythms during imaging and rhyming. In preparation. 1993.

Farah, M.J. The neurological basis of mental imagery: A componential analysis. *Cognition*, 1984, 18, 245-272.

Farah, M.J. Is visual imagery really visual? Overlooked evidence from neuropsychology. *Psychol. Rev.* 1988, 95, 307-317.

Fender, D. in Gevins, A.S. & Remond, A. (Eds.) *Handbook of Electroencephalography and Clinical Neurophysiology:* Vol. 1, Methods of Analysis of Brain Electrical and Magnetic Signals. Elsevier, 1987.

Finke, R.A. and Shepard, R.N., Visual functions of mental imagery. In Boff, K.R., Kaufman, L. and Thomas, J.P. (Eds.), *Handbook of Perception and Human Performance: Vol. II, Cognitive Processes and Performance*, New York, John Wiley and Sons, 1986.

Goldenberg, G., Podreka, I., Uhl, F., Steiner, M., Willmes, K. & Deecke, L. Regional cerebral blood flow patterns in visual imagery. *Neuropsychologia*, 1989, 27, 641-654.

Goldman-Rakic, P.S., Topography of cognition: Parallel distributed networks in primate association cortex. *Ann. Rev. Neurosci.*, 1988, 11, 137-156.

Kaufman, L., Curtis, S., Wang, J.-Z. & Williamson, S.J. Changes in Cortical Activity When Subjects Scan Memory for Tones, *Electroenceph. clin. Neurophysiol.*, 1992a, 82, 266-284

Kaufman, L., Schwartz, B., Salustri, C., and Williamson, S.J., Modulation of Spontaneous Brain Activity During Mental Imagery, *Cogn. Neurosci.*, 1990, 2, 124-132.

Kaufman, L., Cycowicz, Y., Glanzer, M., & Williamson, S.J. Verbal and imaging tasks have different effects on activity of cerebral cortex. Submitted, 1993.

Kosslyn, S.M. Scanning visual images: Some structural implications. *Percept. & Psychophys.* 1973, 14, 90-94.

Kosslyn, S.M., *Image and Mind*, 1980, Cambridge, Harvard Univ. Press.

Kosslyn, S.M., *Ghosts in mind's machine*. 1983, New York, W.W. Norton.

Luber, B., Kaufman, L., Moeller, J. & Williamson, S.J., Lu, Z.-L., Williamson, S.J. & Kaufman, L. Human primary and association cortex have different lifetimes for activation traces. *Brain Res.* 1992, 527, 236-241.

Lu, Z.-L., Williamson, S.J. & Kaufman, L. Physiological measurements predict the lifetime for human auditory memory of a tone. *Science*, 1992,

Naatanen, R. and Picton, T., The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. *Psychophysiol.*, 24: 1987.

Nunez, P., *Electric Field of the Brain*, New York, Oxford Univ. Press, 1987.

Petersen, S.E., Fox, P.T., Posner, M.I., Mintun, M., & Raichle, M.E. Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature*, 1988, 331, 585-589.

Petersen, S.E., Fox, P.T., Posner, M.I., Mintun, M. & Raichle, M.E. Positron emission tomographic studies of the processing of single words. *J. Cog. Neuroscience*, 1989, 2, 153-170.

Petersen, S.E., Fox, P.T., Posner, M.I., Snyder, A.Z., & Raichle, M.E., Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. *Science*, 1990, 1041-1044.

Pylyshyn, Z.W., The imagery debate: Analogue media versus tacit knowledge. *Psychol. Rev. 80: 1-24, 1973.*

Roland, P.E. & Friberg, L. Localization of cortical areas activated by thinking. J. Neurophysiol. 1985, 53, 1219-1243.

Wang, J.-Z., Williamson S.J. & Kaufman L., Magnetic Source Images Determined by a Lead-Field Analysis: The Unique Minimum-Norm Least-Squares Estimation, *IEEE Trans. Biomed. Eng.*, 1992a, 39, 7, 665-675.

Wang, J.-Z., Kaufman, L., & Williamson, S.J. Imaging Regional Changes in the Spontaneous Activity of the Brain: An Extension of the Unique Minimum-Norm Least-Squares Estimate. *Electroenceph. clin. Neurophysiol.*, in press, 1992b.

Wang, J.-Z., Williamson, S.J., & Kaufman, L. Magnetic Source Imaging Based on the Minimum-Norm Least-Squares Inverse. Brain Topography, in press, 1992c.

Wang, J.-Z. Minimum-norm Least-squares Estimation: Magnetic Source Images for a Spherical Model Head, *IEEE Trans. Biomed. Eng.*, in press, 1992a

Wang, J.-Z. MNLS Inverse Discriminates between Neuronal Activity on Opposite Walls of a Sulcus of the Brain, Submitted for publication in IEEE Trans. Biomed. Eng., 1992b.

Williamson, S.J. and Kaufman, L., Magnetic Fields of the Cerebral Cortex. in

Biomagnetism, S.N. Erné, H.D. Hahlbohm and H. Lübbig, eds., Walter de Gruyter & Co., Berlin New York, 353-401, 1981.

Williamson, S.J. and Kaufman, L., Analysis of Neuromagnetic Signals. in: A.S. Gevins and A. Remond (Eds.), *Handbook of Electroenceph. clin. Neurophysil.*, Vol.1. Methods of Analysis of Brain Electrical and Magnetic Signals. Elsevier, Amsterdam, 405-444, 1987.